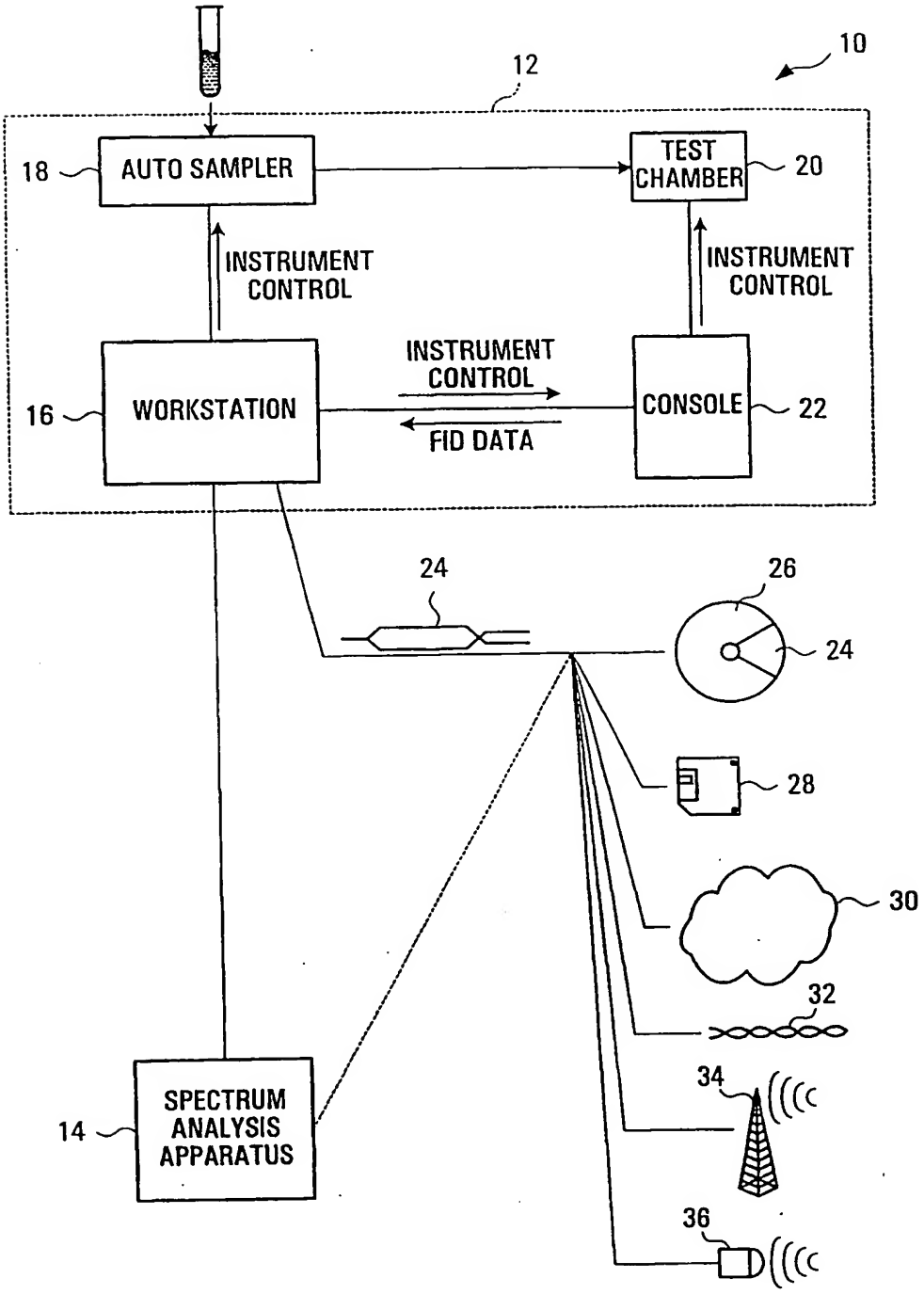

10
12
18
AUTO SAMPLER
TEST CHAMBER
20
INSTRUMENT CONTROL
INSTRUMENT CONTROL
16
WORKSTATION
INSTRUMENT CONTROL
FID DATA
CONSOLE
22
24
26
24
28
30
32
34
36
14
SPECTRUM ANALYSIS APPARATUS

FIG. 1

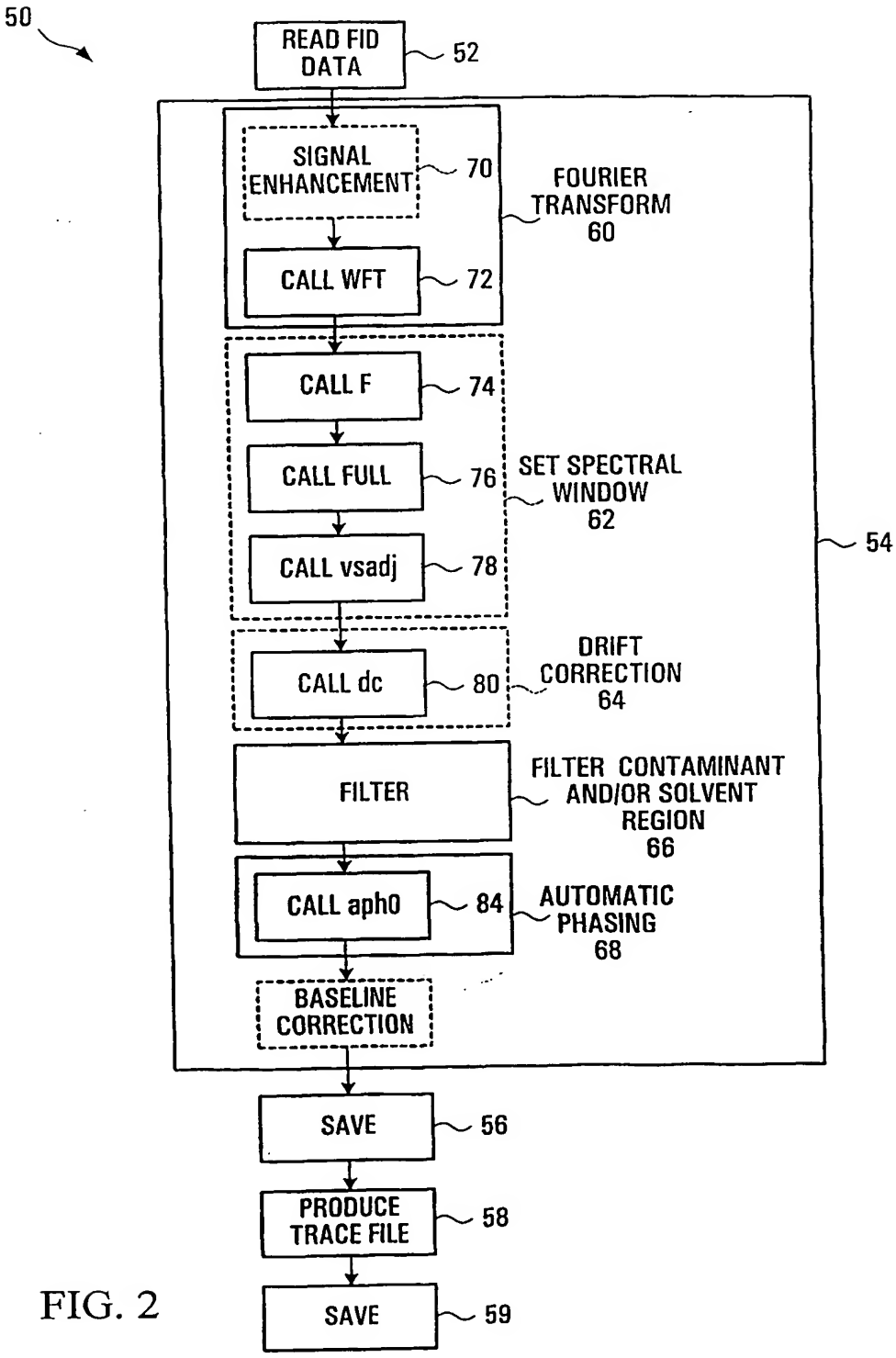
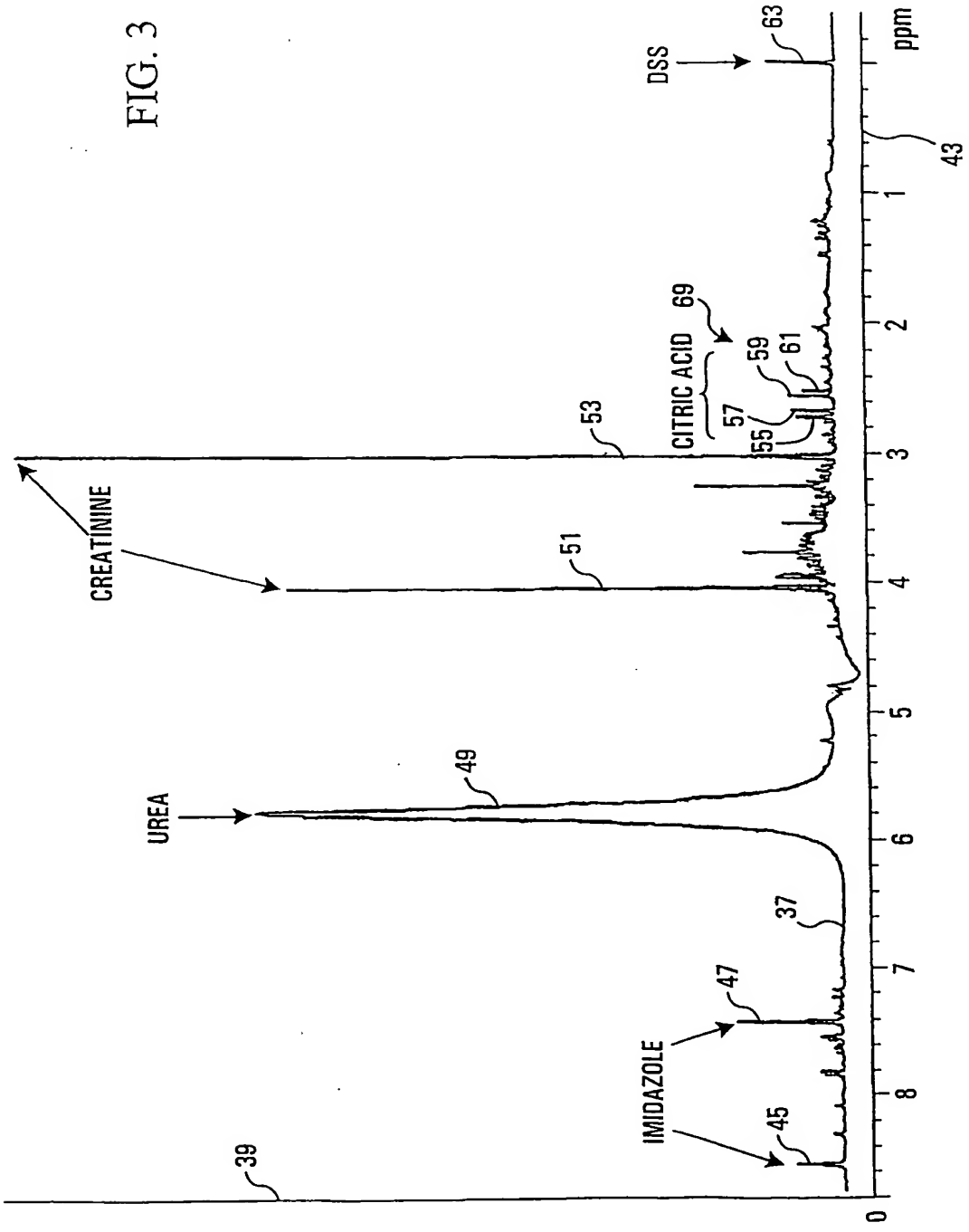

50
READ FID DATA
52
SIGNAL ENHANCEMENT
70
FOURIER TRANSFORM 60
CALL WFT
72
CALL F
74
CALL FULL
76
SET SPECTRAL WINDOW 62
CALL vsadj
78
54
CALL dc
80
DRIFT CORRECTION 64
FILTER
FILTER CONTAMINANT AND/OR SOLVENT REGION 66
CALL aph0
84
AUTOMATIC PHASING 68
BASELINE CORRECTION
SAVE
56
PRODUCE TRACE FILE
58
SAVE
59

FIG. 2

FIG. 3


CREATININE
UREA
IMIDAZOLE
CITRIC ACID
DSS
ppm
0
1
2
3
4
5
6
7
8
39
45
47
37
49
51
53
55
57
59
61
69
63
43

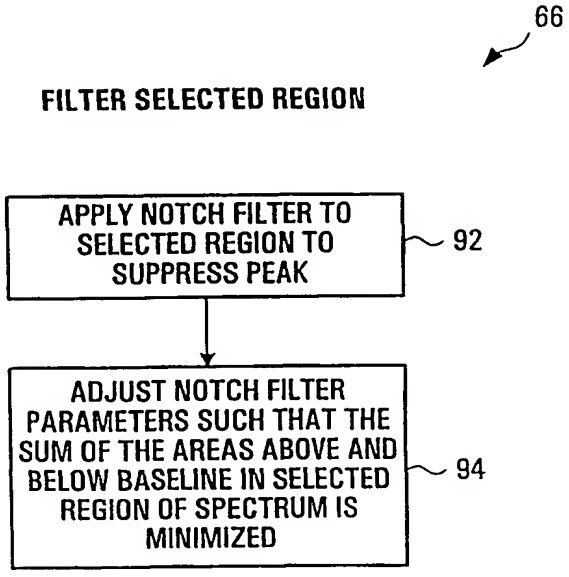

66
FILTER SELECTED REGION
APPLY NOTCH FILTER TO SELECTED REGION TO SUPPRESS PEAK
92
ADJUST NOTCH FILTER PARAMETERS SUCH THAT THE SUM OF THE AREAS ABOVE AND BELOW BASELINE IN SELECTED REGION OF SPECTRUM IS MINIMIZED
94

FIG. 4

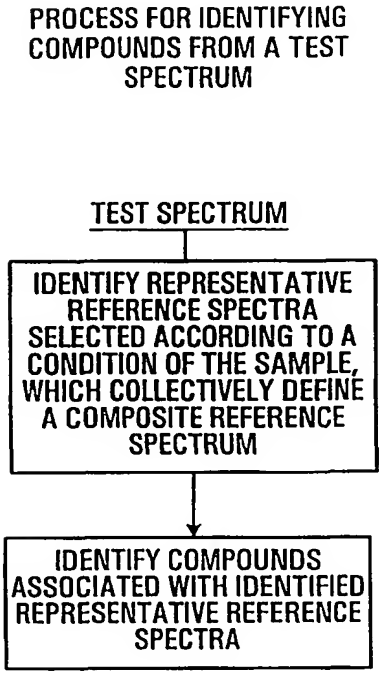
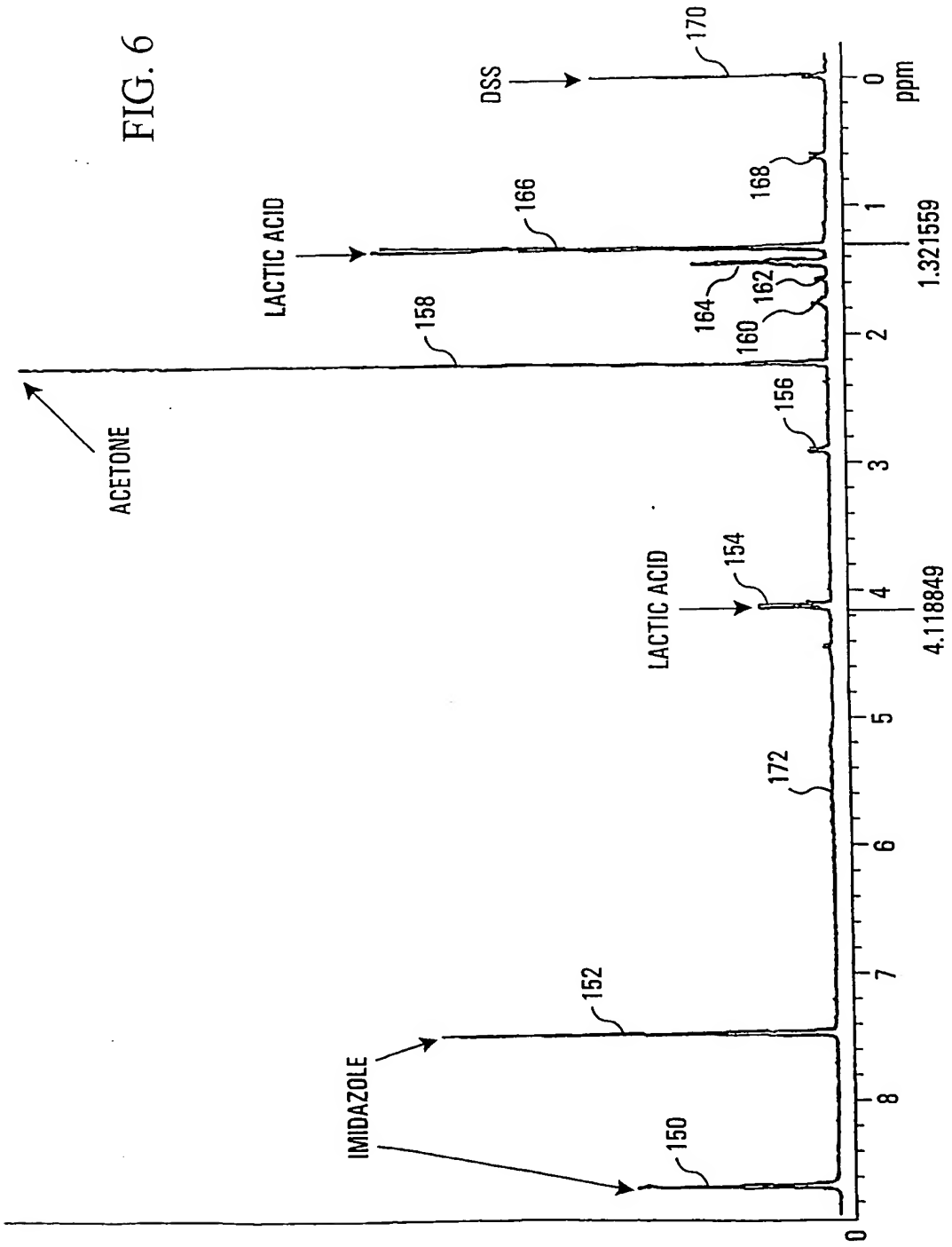

PROCESS FOR IDENTIFYING COMPOUNDS FROM A TEST SPECTRUM
TEST SPECTRUM
IDENTIFY REPRESENTATIVE REFERENCE SPECTRA SELECTED ACCORDING TO A CONDITION OF THE SAMPLE, WHICH COLLECTIVELY DEFINE A COMPOSITE REFERENCE SPECTRUM
IDENTIFY COMPOUNDS ASSOCIATED WITH IDENTIFIED REPRESENTATIVE REFERENCE SPECTRA

FIG. 5

FIG. 6


ACETONE
LACTIC ACID
LACTIC ACID
IMIDAZOLE
DSS
158
166
168
164
160
162
156
154
172
152
150
170
1.321559
4.118849
ppm
0
1
2
3
4
5
6
7
8

```
REAL SPECTRAL DATA - pH=5.10
<?xml version="1.0"?>
<!--compoundDB version="2.0"-->
<compound>                                                          } 200
  <name>LacticAcid</name>
  <molecularWeight>90.08</molecularWeight>

  <experiment>
  <pH>5.1</pH>
  <temperatureKelvin>298.150000</temperatureKelvin>
  <DSSRatio>0.533668</DSSRatio>
  <concentration>4.308710</concentration>                           } 202
  <timestamp>Sept 5 2001</timestamp>
  <sourceFID>lacticacid.fid</sourceFID>
  <magnetMHz>400.120773</magnetMHz>
  <spectralWidthHz>6006.006006</spectralWidthHz>
</experiment>

    <cluster>                                                       } 204
                                                    206 ↙
210 ➝ <protonNumber>3</protonNumber>
212 ➝ <quantification>1</quantification>
      <subCluster>
        <centerPPM>1.321559</centerPPM>
214 ➝ <lorentzianWidthAdjust>2.893258</lorentzianWidthAdjust>
        <peak>                                                      } 216
220 ➝ <offsetCenterHz>-3.455480</offsetCenterHz>
222 ➝ <height>0.988680</height>
224 ➝ <protonRatio>1.491461</protonRation>
        </peak>
        <peak>                                                      } 218
          <offsetCenterHz>3.455480</offsetCenterHz>
          <height>1.0000000</height>
          <protonRation>1.508539</protonRatio>
        </peak>
      </subCluster>
    </cluster>
```

FIG. 7A

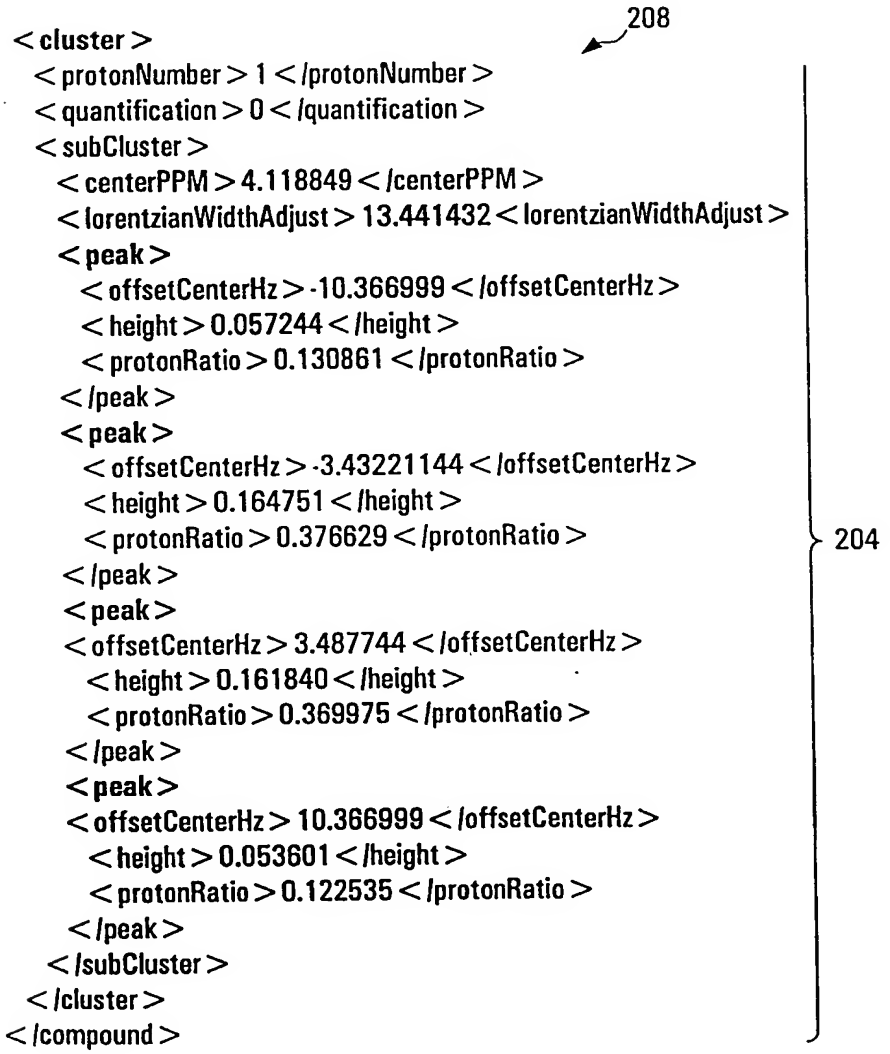

208
<cluster>
<protonNumber>1</protonNumber>
<quantification>0</quantification>
<subCluster>
<centerPPM>4.118849</centerPPM>
<lorentzianWidthAdjust>13.441432</lorentzianWidthAdjust>
<peak>
<offsetCenterHz>-10.366999</offsetCenterHz>
<height>0.057244</height>
<protonRatio>0.130861</protonRatio>
</peak>
<peak>
<offsetCenterHz>-3.43221144</offsetCenterHz>
<height>0.164751</height>
<protonRatio>0.376629</protonRatio>
</peak>
<peak>
<offsetCenterHz>3.487744</offsetCenterHz>
<height>0.161840</height>
<protonRatio>0.369975</protonRatio>
</peak>
<peak>
<offsetCenterHz>10.366999</offsetCenterHz>
<height>0.053601</height>
<protonRatio>0.122535</protonRatio>
</peak>
</subCluster>
</cluster>
</compound>
204

FIG. 7B

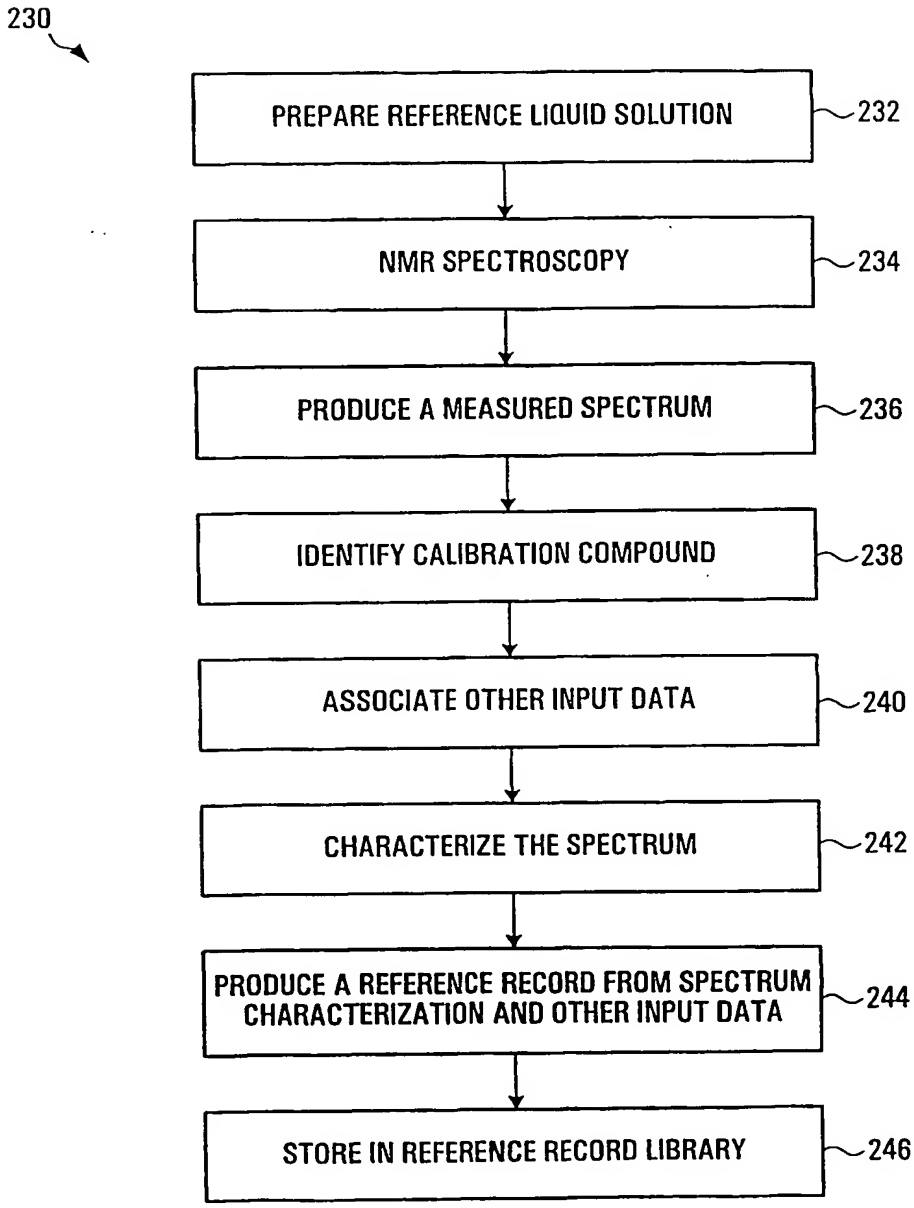

230
PREPARE REFERENCE LIQUID SOLUTION
232
NMR SPECTROSCOPY
234
PRODUCE A MEASURED SPECTRUM
236
IDENTIFY CALIBRATION COMPOUND
238
ASSOCIATE OTHER INPUT DATA
240
CHARACTERIZE THE SPECTRUM
242
PRODUCE A REFERENCE RECORD FROM SPECTRUM CHARACTERIZATION AND OTHER INPUT DATA
244
STORE IN REFERENCE RECORD LIBRARY
246

FIG. 8

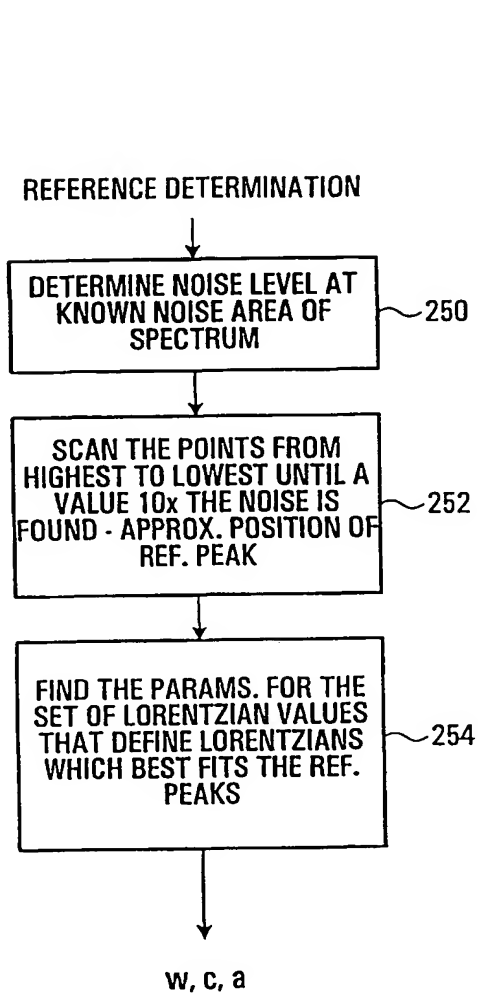

238
REFERENCE DETERMINATION
DETERMINE NOISE LEVEL AT KNOWN NOISE AREA OF SPECTRUM
250
SCAN THE POINTS FROM HIGHEST TO LOWEST UNTIL A VALUE 10x THE NOISE IS FOUND - APPROX. POSITION OF REF. PEAK
252
FIND THE PARAMS. FOR THE SET OF LORENTZIAN VALUES THAT DEFINE LORENTZIANS WHICH BEST FITS THE REF. PEAKS
254
w, c, a

FIG. 9

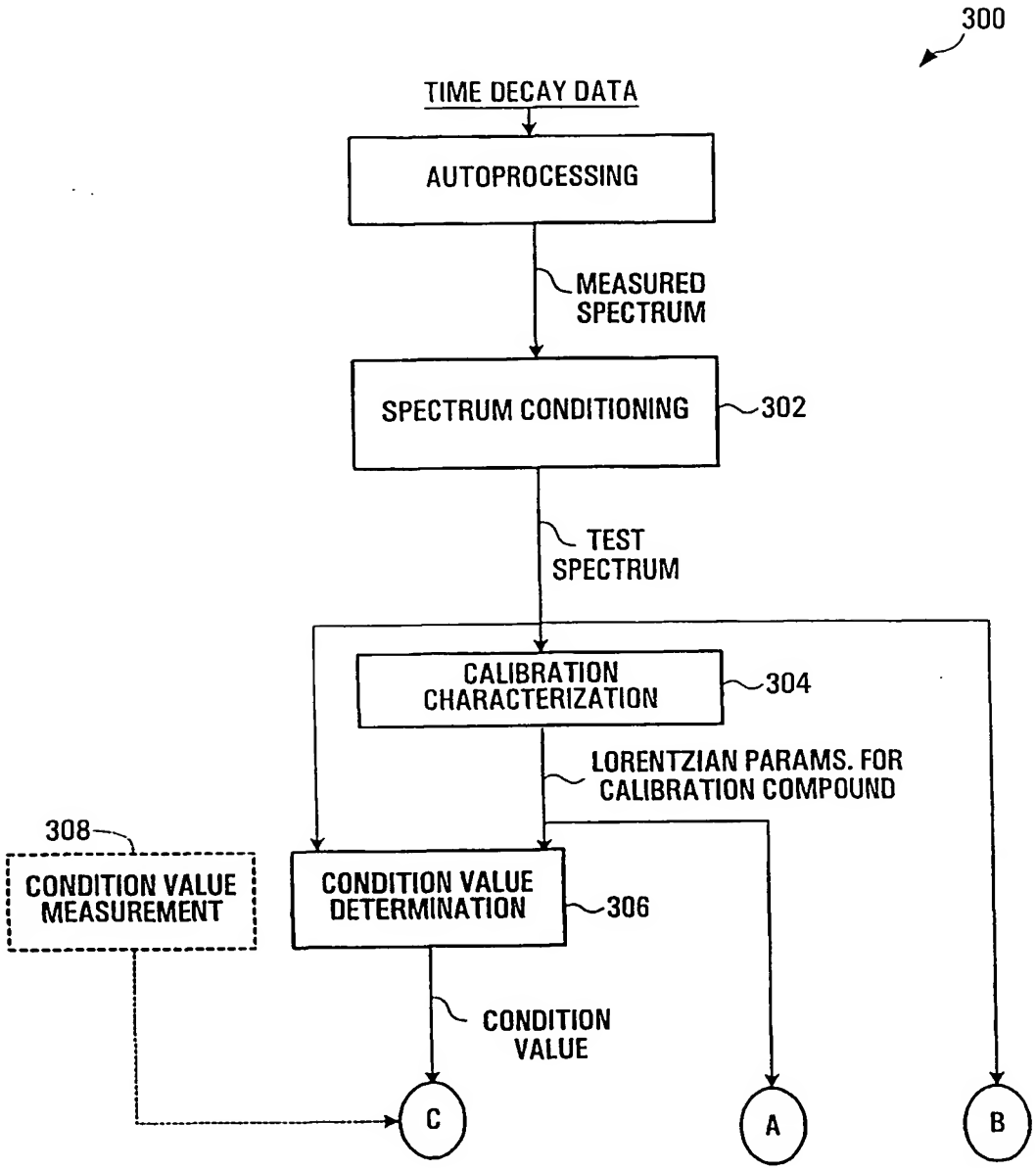

300
TIME DECAY DATA
AUTOPROCESSING
MEASURED SPECTRUM
SPECTRUM CONDITIONING
302
TEST SPECTRUM
CALIBRATION CHARACTERIZATION
304
LORENTZIAN PARAMS. FOR CALIBRATION COMPOUND
308
CONDITION VALUE MEASUREMENT
CONDITION VALUE DETERMINATION
306
CONDITION VALUE
C
A
B

FIG. 10A

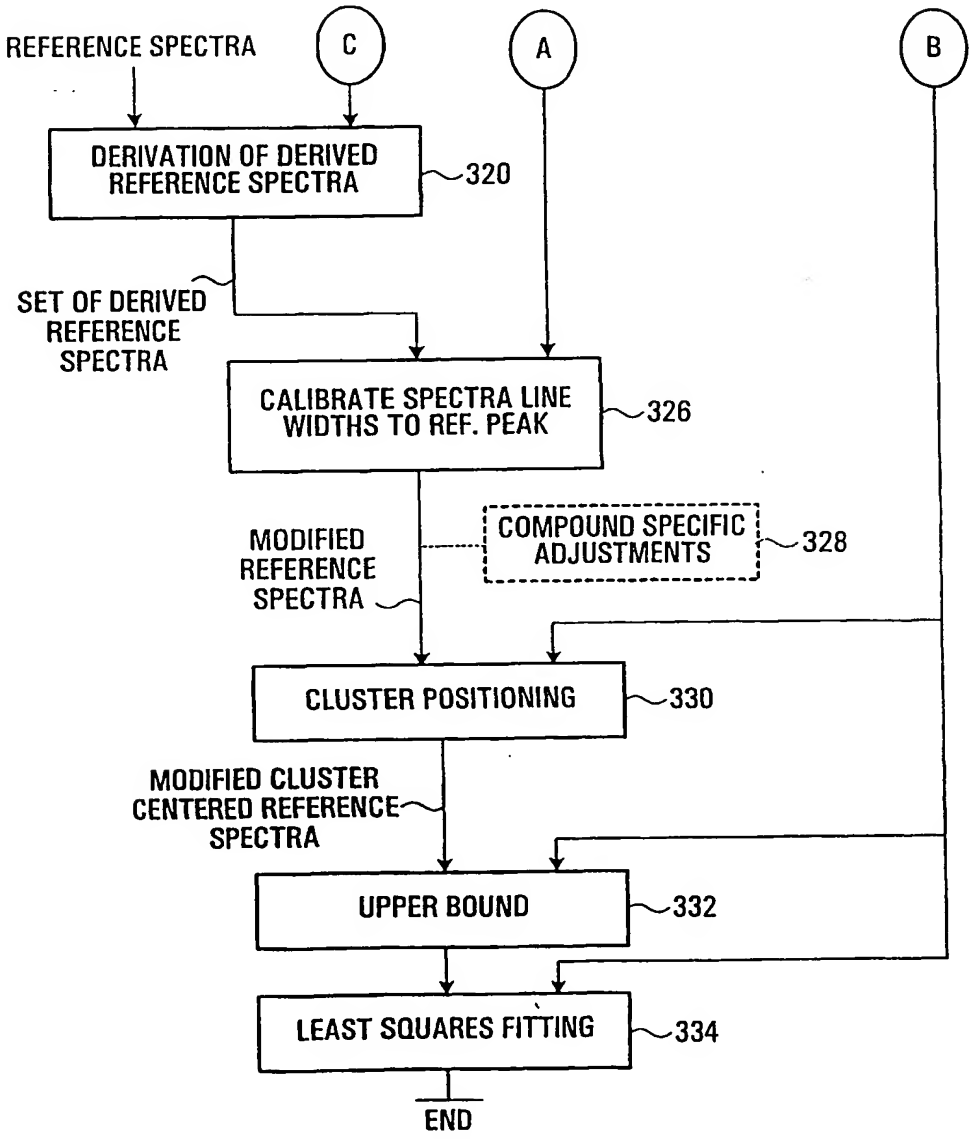

REFERENCE SPECTRA
C
A
B
DERIVATION OF DERIVED REFERENCE SPECTRA
320
SET OF DERIVED REFERENCE SPECTRA
CALIBRATE SPECTRA LINE WIDTHS TO REF. PEAK
326
MODIFIED REFERENCE SPECTRA
COMPOUND SPECIFIC ADJUSTMENTS
328
CLUSTER POSITIONING
330
MODIFIED CLUSTER CENTERED REFERENCE SPECTRA
UPPER BOUND
332
LEAST SQUARES FITTING
334
END

FIG. 10B

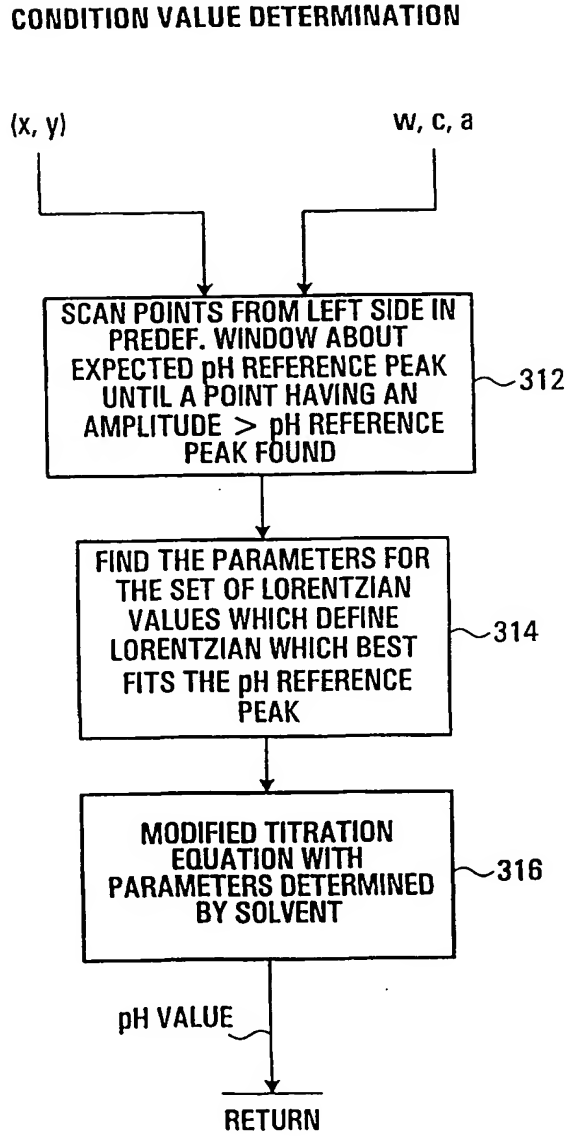

CONDITION VALUE DETERMINATION
310
(x, y)
w, c, a
SCAN POINTS FROM LEFT SIDE IN PREDEF. WINDOW ABOUT EXPECTED pH REFERENCE PEAK UNTIL A POINT HAVING AN AMPLITUDE > pH REFERENCE PEAK FOUND
312
FIND THE PARAMETERS FOR THE SET OF LORENTZIAN VALUES WHICH DEFINE LORENTZIAN WHICH BEST FITS THE pH REFERENCE PEAK
314
MODIFIED TITRATION EQUATION WITH PARAMETERS DETERMINED BY SOLVENT
316
pH VALUE
RETURN

FIG. 11

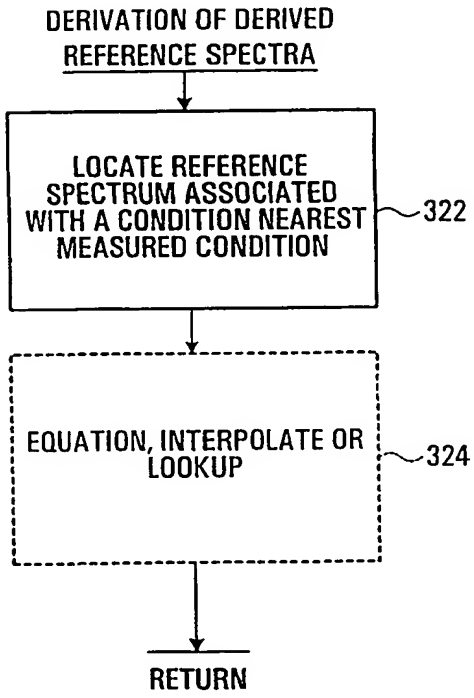

DERIVATION OF DERIVED REFERENCE SPECTRA
LOCATE REFERENCE SPECTRUM ASSOCIATED WITH A CONDITION NEAREST MEASURED CONDITION
322
EQUATION, INTERPOLATE OR LOOKUP
324
RETURN

FIG. 12

Real Spectral Data - pH=5.45

```
<?xml version="1.0"?>
<!-- compoundDB version="2.0" -->
<compound>
 <name>LacticAcid</name>
 <molecularWeight>90.08</molecularWeight>


 <experiment>
  <pH>5.45</pH>
  <temperatureKelvin>298.150000</temperatureKelvin>
  <DSSRatio>0.533668</DSSRatio>
  <concentration>4.308710</concentration>
  <timestamp>Sept 5 2001</timestamp>
  <sourceFID>lacticacid.fid</sourceFID>
  <magnetMHz>400.120699</magnetMHz>
  <spectralWidthHz>6006.006006</spectralWidthHz>
 </experiment>


 <cluster>
  <protonNumber>3</protonNumber>
  <quantification>1</quantification>
  <subCluster>
   <centerPPM>1.318770</centerPPM>
   <lorentzianWidthAdjust>1.562004</lorentzianWidthAdjust>
   <peak>
    <offsetCenterHz>-3.453329</offsetCenterHz>
    <height>0.983656</height>
    <protonRatio>1.487641</protonRatio>
   </peak>
   <peak>
    <offsetCenterHz>3.453329</offsetCenterHz>
    <height>1.000000</height>
    <protonRatio>1.512359</protonRatio>
   </peak>
  </subCluster>
 </cluster>
```

FIG. 13A

```
<cluster>
  <protonNumber>1</protonNumber>
  <quantification>0</quantification>
  <subCluster>
    <centerPPM>4.110990</centerPPM>
    <lorentzianWidthAdjust>7.044502</lorentzianWidthAdjust>
    <peak>
      <offsetCenterHz>-10.371092</offsetCenterHz>
      <height>0.054671</height>
      <protonRatio>0.124148</protonRatio>
    </peak>
    <peak>
      <offsetCenterHz>-3.448909</offsetCenterHz>
      <height>0.164509</height>
      <protonRatio>0.373572</protonRatio>
    </peak>
    <peak>
      <offsetCenterHz>3.456819</offsetCenterHz>
      <height>0.163879</height>
      <protonRatio>0.372141</protonRatio>
    </peak>
    <peak>
      <offsetCenterHz>10.371092</offsetCenterHz>
      <height>0.057309</height>
      <protonRatio>0.130139</protonRatio>
    </peak>
  </subCluster>
</cluster>
</compound>
```

FIG. 13B

Interpolated Data - pH=5.28

```
<?xml version="1.0"?>
<!-- compoundDB version="2.0" -->
<compound>
 <name>LacticAcid</name>
 <molecularWeight>90.08</molecularWeight>


 <experiment>
  <pH>5.45</pH>
  <temperatureKelvin>298.150000</temperatureKelvin> : copied
  <DSSRatio>0.533668</DSSRatio>
  <concentration>4.308710</concentration>
  <timestamp>Sept 5 2001</timestamp>
  <sourceFID>lacticacid.fid</sourceFID> :copied
  <magnetMHz>400.120699</magnetMHz>
  <spectralWidthHz>6006.006006</spectralWidthHz>
 </experiment>


 <cluster>
  <protonNumber>3</protonNumber>
  <quantification>1</quantification>
  <subCluster>
   <centerPPM>1.3202</centerPPM> : interpolated
   <lorentzianWidthAdjust>1.562004</lorentzianWidthAdjust>
   <peak>
    <offsetCenterHz>-3.453329</offsetCenterHz>
    <height>0.983656</height>
    <protonRatio>1.487641</protonRatio>
   </peak>
   <peak>
    <offsetCenterHz>3.453329</offsetCenterHz>
    <height>1.000000</height>
    <protonRatio>1.512359</protonRatio>
   </peak>
  </subCluster>
 </cluster>
```

FIG. 14A

```
<cluster>
  <protonNumber>1</protonNumber>
  <quantification>0</quantification>
  <subCluster>
   <centerPPM>4.1149</centerPPM> :interpolated
   <lorentzianWidthAdjust>7.044502</lorentzianWidthAdjust>
   <peak>
    <offsetCenterHz>-10.371092</offsetCenterHz>
    <height>0.054671</height>
    <protonRatio>0.124148</protonRatio>
   </peak>
   <peak>
    <offsetCenterHz>-3.448909</offsetCenterHz>
    <height>0.164509</height>
    <protonRatio>0.373572</protonRatio>
   </peak>
   <peak>
    <offsetCenterHz>3.456819</offsetCenterHz>
    <height>0.163879</height>
    <protonRatio>0.372141</protonRatio>
   </peak>
   <peak>
    <offsetCenterHz>10.371092</offsetCenterHz>
    <height>0.057309</height>
    <protonRatio>0.130139</protonRatio>
   </peak>
  </subCluster>
 </cluster>
</compound>
```

FIG. 14B

Generic Lactic Acid record

```
<?xml version="1.0"?>
<!-- compoundDB version="2.0" -->
<compound>
 <name>LacticAcid</name>
 <molecularWeight>90.08</molecularWeight>


 <experiment>
  <pH>5.45</pH>
  <temperatureKelvin>298.150000</temperatureKelvin>
  <DSSRatio>0.533668</DSSRatio>
  <concentration>4.308710</concentration>
  <timestamp>Sept 5 2001</timestamp>
  <sourceFID>lacticacid.fid</sourceFID>
  <magnetMHz>400.120699</magnetMHz>
  <spectralWidthHz>6006.006006</spectralWidthHz>
 </experiment>


 <cluster>
  <protonNumber>3</protonNumber>
  <quantification>1</quantification>
  <subCluster>
   <centerPPM>y=m1(pH)+b1</centerPPM>
   <lorentzianWidthAdjust>1.562004</lorentzianWidthAdjust>
   <peak>
    <offsetCenterHz>-3.453329</offsetCenterHz>
    <height>0.983656</height>
    <protonRatio>1.487641</protonRatio>
   </peak>
   <peak>
    <offsetCenterHz>3.453329</offsetCenterHz>
    <height>1.000000</height>
    <protonRatio>1.512359</protonRatio>
   </peak>
  </subCluster>
 </cluster>
```

FIG. 15A

```
<cluster>
  <protonNumber>1</protonNumber>
  <quantification>0</quantification>
  <subCluster>
   <centerPPM> y=m2(pH)+b2 </centerPPM>
   <lorentzianWidthAdjust>7.044502</lorentzianWidthAdjust>
   <peak>
    <offsetCenterHz>-10.371092</offsetCenterHz>
    <height>0.054671</height>
    <protonRatio>0.124148</protonRatio>
   </peak>
   <peak>
    <offsetCenterHz>-3.448909</offsetCenterHz>
    <height>0.164509</height>
    <protonRatio>0.373572</protonRatio>
   </peak>
   <peak>
    <offsetCenterHz>3.456819</offsetCenterHz>
    <height>0.163879</height>
    <protonRatio>0.372141</protonRatio>
   </peak>
   <peak>
    <offsetCenterHz>10.371092</offsetCenterHz>
    <height>0.057309</height>
    <protonRatio>0.130139</protonRatio>
   </peak>
  </subCluster>
 </cluster>
</compound>
```

FIG. 15B

Generic Lactic Acid record with Lookup Table link

```
<?xml version="1.0"?>
<!-- compoundDB version="2.0" -->
<compound>
 <name>LacticAcid</name>
 <molecularWeight>90.08</molecularWeight>


 <experiment>
  <pH>5.45</pH>
  <temperatureKelvin>298.150000</temperatureKelvin>
  <DSSRatio>0.533668</DSSRatio>
  <concentration>4.308710</concentration>
  <timestamp>Sept 5 2001</timestamp>
  <sourceFID>lacticacid.fid</sourceFID>
  <magnetMHz>400.120699</magnetMHz>
  <spectralWidthHz>6006.006006</spectralWidthHz>
 </experiment>


 <cluster>
  <protonNumber>3</protonNumber>
  <quantification>1</quantification>
  <subCluster>
   <centerPPM>LOOKUP TABLE LINK1</centerPPM>
   <lorentzianWidthAdjust>1.562004</lorentzianWidthAdjust>
   <peak>
    <offsetCenterHz>-3.453329</offsetCenterHz>
    <height>0.983656</height>
    <protonRatio>1.487641</protonRatio>
   </peak>
   <peak>
    <offsetCenterHz>3.453329</offsetCenterHz>
    <height>1.000000</height>
    <protonRatio>1.512359</protonRatio>
   </peak>
  </subCluster>
 </cluster>
```

FIG. 16A

```
<cluster>
  <protonNumber>1</protonNumber>
  <quantification>0</quantification>
  <subCluster>
   <centerPPM> LOOKUP TABLE LINK2 </centerPPM>
   <lorentzianWidthAdjust>7.044502</lorentzianWidthAdjust>
   <peak>
    <offsetCenterHz>-10.371092</offsetCenterHz>
    <height>0.054671</height>
    <protonRatio>0.124148</protonRatio>
   </peak>
   <peak>
    <offsetCenterHz>-3.448909</offsetCenterHz>
    <height>0.164509</height>
    <protonRatio>0.373572</protonRatio>
   </peak>
   <peak>
    <offsetCenterHz>3.456819</offsetCenterHz>
    <height>0.163879</height>
    <protonRatio>0.372141</protonRatio>
   </peak>
   <peak>
    <offsetCenterHz>10.371092</offsetCenterHz>
    <height>0.057309</height>
    <protonRatio>0.130139</protonRatio>
   </peak>
  </subCluster>
 </cluster>
</compound>
```

FIG. 16B

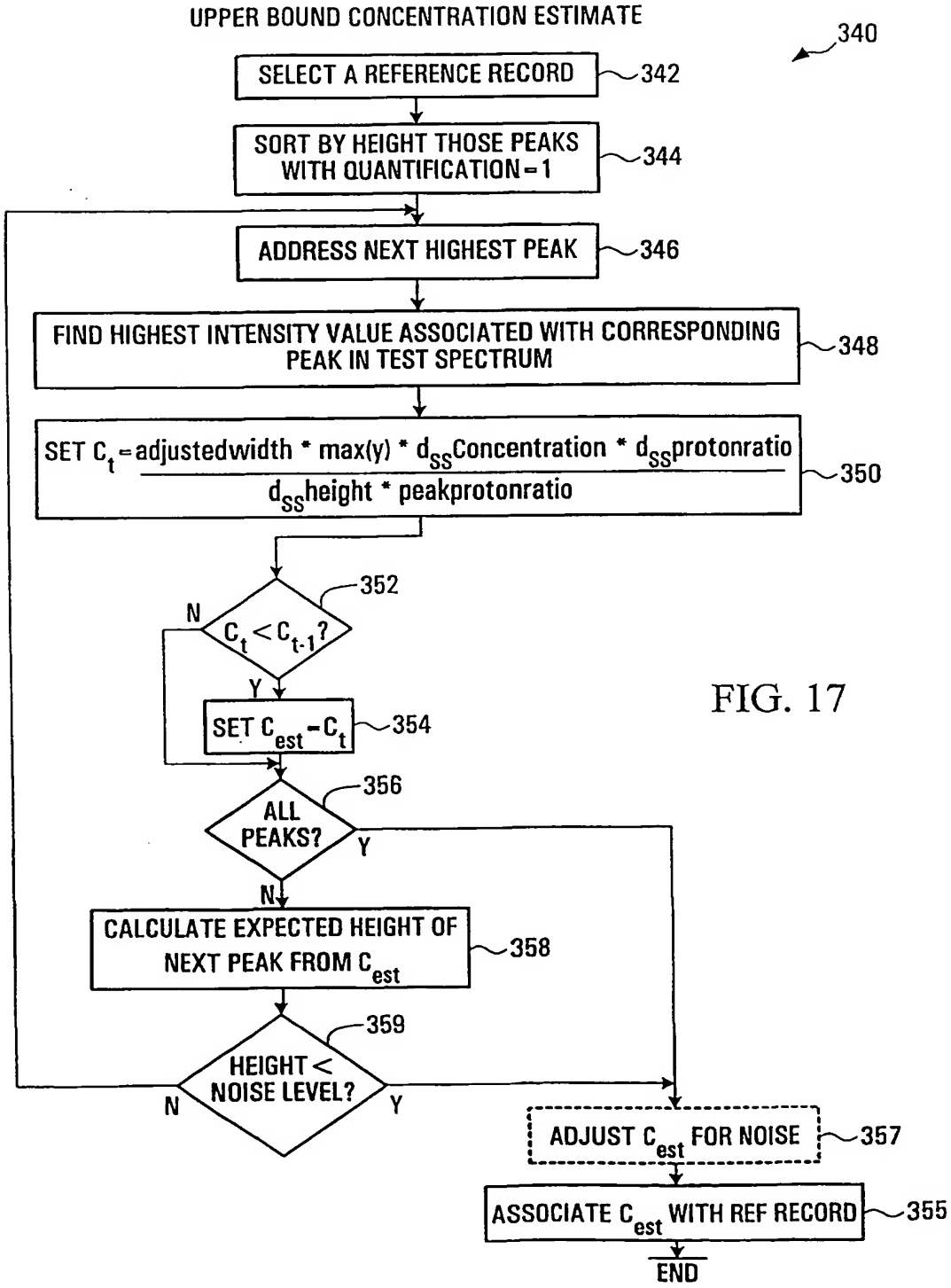

UPPER BOUND CONCENTRATION ESTIMATE
340
SELECT A REFERENCE RECORD
342
SORT BY HEIGHT THOSE PEAKS WITH QUANTIFICATION=1
344
ADDRESS NEXT HIGHEST PEAK
346
FIND HIGHEST INTENSITY VALUE ASSOCIATED WITH CORRESPONDING PEAK IN TEST SPECTRUM
348
SET C_t = adjustedwidth * max(y) * d_{SS}Concentration * d_{SS}protonratio / d_{SS}height * peakprotonratio
350
352
N
$C_t < C_{t-1}$?
Y
SET $C_{est} = C_t$
354
356
ALL PEAKS?
Y
N
CALCULATE EXPECTED HEIGHT OF NEXT PEAK FROM C_{est}
358
359
HEIGHT < NOISE LEVEL?
N
Y
ADJUST C_{est} FOR NOISE
357
ASSOCIATE C_{est} WITH REF RECORD
355
END

FIG. 17

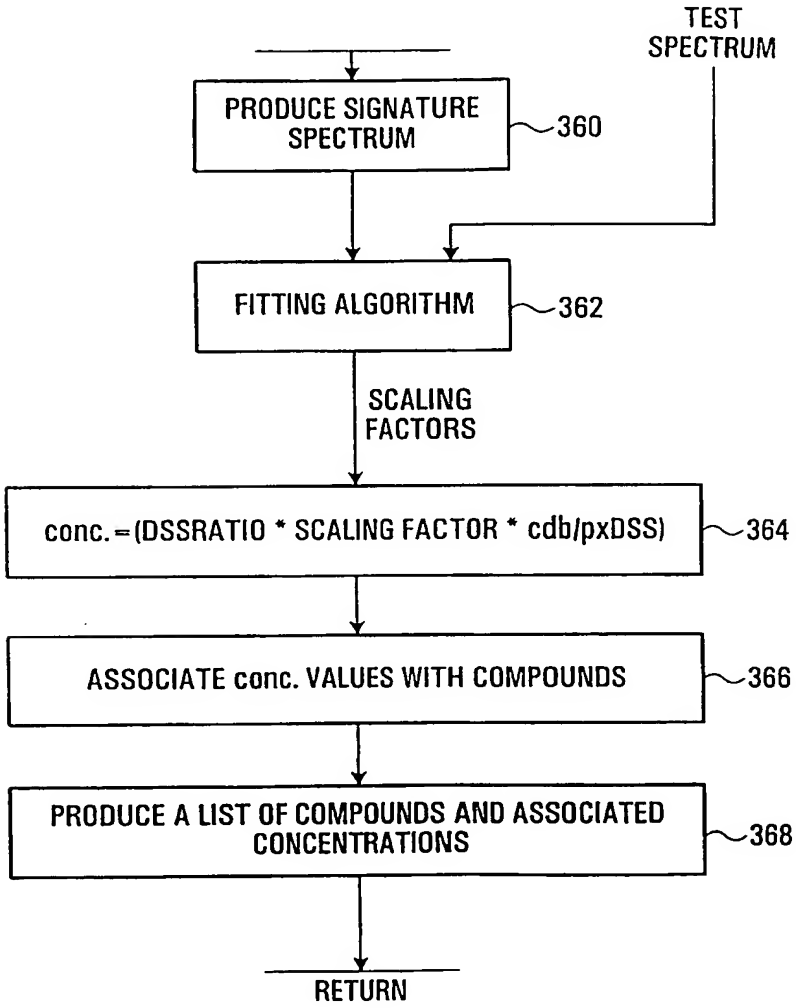

TEST SPECTRUM
PRODUCE SIGNATURE SPECTRUM
360
FITTING ALGORITHM
362
SCALING FACTORS
conc.=(DSSRATIO * SCALING FACTOR * cdb/pxDSS)
364
ASSOCIATE conc. VALUES WITH COMPOUNDS
366
PRODUCE A LIST OF COMPOUNDS AND ASSOCIATED CONCENTRATIONS
368
RETURN

FIG. 18